

Claim 1. (Amended): A process for preparing 5-(α -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-ones comprising:

(a) reacting

(i) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent and a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or

(ii) 8-hydroxy-(1*H*)-quinolin-2-one with an acylating agent to form 8-acetoxy-(1*H*)-quinolin-2-one, and treating, in-situ, the 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one; or

~~(iii) 8-acetoxy-(1*H*)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one;~~

(b) reacting the 5-acetyl-8-hydroxy-(1*H*)-quinolin-2-one prepared in Step (a) with a compound having the Formula RL in the presence of a base and a solvent to form 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one, wherein R is a protecting group and L is a leaving group; and

(c) reacting the 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one with a halogenating agent in the presence of a solvent to form a 5-(α -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one.

Claim 2. (Previously presented): A process according to Claim 1 is present in an amount of from 1 molar equivalents to 1.5 molar equivalents, based on the molar equivalents of 8-hydroxy-(1*H*)-quinolin-2-one.

Claim 3. (Previously presented): A process according to Claim 1, wherein the Lewis acid is present in an amount of from 3 molar equivalents to 5 molar equivalents, based on the molar equivalents of 8-hydroxy-(1*H*)-quinolin-2-one or on the molar equivalents of 8-acetoxy-(1*H*)-quinolin-2-one.

Claim 4. (Previously presented): A process according to Claim 1, wherein Step (a) is conducted in the presence of an alkaline halide selected from the group consisting of sodium chloride, sodium bromide, lithium chloride and lithium bromide.

Claim 5. (Previously presented): A process according to Claim 1, wherein the compound having the Formula RL is selected from the group consisting of α -methylbenzyl bromide, methyl chloride, benzylchloride and benzylbromide.

Claim 6 (Previously presented): A process according to Claims 1, wherein the 5-acetyl-8-substituted oxy-(1*H*)-quinolin-2-one is 5-acetyl-8-benzyloxy-(1*H*)-quinolin-2-one.

Claim 7 (Previously presented): A process according to Claim 1, wherein the halogenating agent is selected from the group consisting of sodium bromate and hydrobromic acid, bromine, *N*-bromosuccinimide, *N*-chlorosuccinimide, iodine, chlorine, sulfuryl chloride, benzyltrimethylammoniumdichloro-iodate, copper chloride, pyridinium tribromide, tetraalkylammonium tribromide, iodine chloride, hydrochloric acid and an oxidating agent and combinations thereof.

Claim 8 (Original): A process according to Claim 7, wherein the halogenating agent is benzyltrimethyl-ammoniumdichloroiodate.

Claim 9 (Previously presented): A process according to Claims 1, wherein the 5-(α -haloacetyl)-8-substituted oxy-(1*H*)-quinolin-2-one is 5-(α -chloroacetyl)-8-benzyloxy-(1*H*)-quinolin-2-one.

Claim 10 (Previously presented): A process according to Claim 1, wherein in Step (a) the solvent is selected from the group consisting of methylenechloride, 1,2-ethylene dichloride, chlorobenzene, *o*-dichloro-benzene, aliphatic C₈-C₁₂-hydrocarbons and combinations thereof; in Step (b) the solvent is selected from the group consisting of acetone, methyl isobutyl ketone, tetrahydrofuran, diisopropyl ether, 2-methoxyethyl ether, diethylene ether, methylenechloride, water and combinations thereof; and in Step (c) the solvent is selected from the group consisting of acetic acid, trifluoroacetic acid, propionic acid; ethyl acetate, isopropyl acetate, butyl acetate, toluene, benzene, tetrahydrofuran, diisopropyl ether, 2-methoxyethyl ether, diethylene ether, methylenechloride and combinations thereof.

Claim 11 (Previously presented): A process according to Claim 1, wherein in Step (a) the temperature is from 0 °C to 160 °C; in Step (b) the temperature is from 20 °C to 90 °C; and in Step (c) the temperature is from about 10 °C to about 160 °C.

Claim 12 (Amended):: A process for preparing 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1H)-quinolinone-2-one salts comprising:

(a) reacting

(i) 8-hydroxy-(1H)-quinolin-2-one with an acylating agent and a Lewis acid to form 5-acetyl-8-hydroxy-(1H)-quinolin-2-one; or

(ii) 8-hydroxy-(1H)-quinolin-2-one with an acylating agent to form 8-acetoxy-(1H)-quinolin-2-one, and treating, in-situ, the 8-acetoxy-(1H)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1H)-quinolin-2-one; or

~~(iii) 8-acetoxy-(1H)-quinolin-2-one with a Lewis acid to form 5-acetyl-8-hydroxy-(1H)-quinolin-2-one;~~

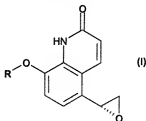
(b) reacting the 5-acetyl-8-hydroxy-(1H)-quinolin-2-one prepared in Step (i) with a compound having the Formula RL in the presence of a base and a solvent to form 5-acetyl-8-substituted oxy-(1H)-quinolin-2-one, wherein R is a protecting group and L is a leaving group;

(c) reacting the 5-acetyl-8-substituted oxy-(1H)-quinolin-2-one with a halogenating agent in the presence of a solvent to form a 5-(α -haloacetyl)-8-substituted oxy-(1H)-quinolin-2-one;

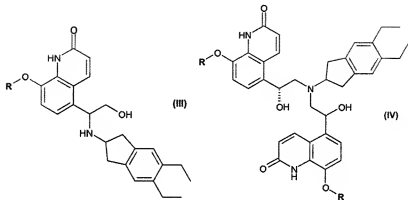
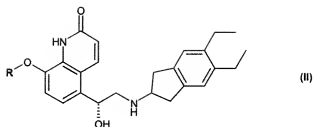
(d) reacting an 5-(α -haloacetyl)-8-substituted oxy-(1H)-quinolin-2-one with a reducing agent in the presence of a chiral catalyst to form 8-(substituted oxy)-5-[(R)-2-halo-1-hydroxy-ethyl]-(1H)-quinolin-2-one;

(e) treating the 8-(substituted oxy)-5-[(R)-2-halo-1-hydroxy-ethyl]-(1H)-quinolin-2-one with a base in the presence of a solvent to form 8-(substituted oxy)-5-(R)-oxiranyl-(1H)-quinolin-2-one;

(f) reacting the 8-substituted oxy-5-(R)-oxiranyl-(1H)-quinolin-2-one having Formula (I)



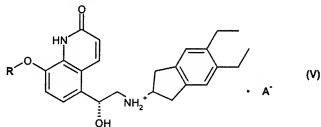
with 2-amino-(5-6-diethyl)-indan to form a reaction mixture containing compounds having Formulae (II), (III) and (IV)



wherein R is a protecting group;

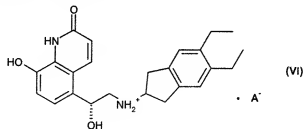
(g) treating the reaction mixture prepared in Step (i) with an acid in the presence of a solvent to form a corresponding salt;

(h) isolating and crystallizing a salt having Formula (V)



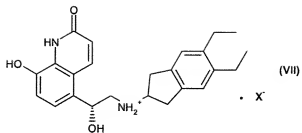
wherein R is a protecting group and A⁻ is an anion;

(i) removing the protecting group from the salt having Formula (V) in the presence of a solvent to form a salt having Formula (VI):



wherein A⁻ is an anion; and

(j) treating the salt having Formula (VI) with an acid in the presence of a solvent to form 5-[(R)-2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-(1*H*)-quinolin-2-one salt having Formula (VII)



wherein X^- is an anion.

Claim 13 (Previously presented): A process according to Claim 2, wherein the acylating agent is acetic anhydride or acetyl chloride.

Claim 14 (Previously presented): A process according to Claim 4, wherein the Lewis acid is selected from the group consisting of boron trifluoride, aluminium chloride or titanium tetrachloride.

Claim 15 (Previously presented): A process according to Claim 4, wherein Step (a) is conducted in the presence of an ionic liquid selected from the group consisting of an imidazolium salt, pyridium salt, ammonium salt, phosphonium salt and sulphonium salt.